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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,975	01/18/2002	Limin Li	STAN-216	5176

23552 7590 12/20/2006
MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/20/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/053,975	LI ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-16,22-25,31,32 and 37-50* is/are pending in the application.

4a) Of the above claim(s) *7-16, 22-25, 31-32, 37-42 and 44--45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-6, 43 and 46-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to the Amendment

The Amendment filed on 09/28/2006 in response to the previous Non-Final Office Action (6/01/2006) is acknowledged and has been entered.

Claims 1, 4-16, 22-25, 31-32 and 37-50 are currently pending.

Claims 7-16, 22-25, 31-32, 37-42 and 44--45 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1, 4-6, 43 and 46-50 are currently pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 6 and 43 **remain** rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (IDS, US 5,891,668, 1999).

Li. et al. teach antibodies which have been raised to normal or mutated forms of TSG101 (column 8, line 59-63). Specifically, the patent teaches antibodies that specifically recognize the coiled domain, leucine zipper and proline rich domains of TSG101 (column 8, lines 64 to column 9, line 4). With regards to TSG101, Li et al. provide both the mouse TSG101 and the human homolog (column 3, lines 26-38, see below, human homolog). Although the reference does not specifically teach that the antibody binds to a polypeptide comprising a ubiquitination-regulating domain, the claims are drawn to the product *per se* and inherently, such an antibody would bind to a polypeptide comprising a ubiquitination-regulating domain. Thus, the claimed peptide appears to be the same as

the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

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Patent No. 5891668
APPLICANT:  LI, Limin
APPLICANT:  COHEN, Stanley N
US-08-670-274B-4

  Query Match             97.8%;  Score 2002;  DB 2;  Length 380;
  Best Local Similarity   100.0%;  Pred. No. 3e-155;
  Matches  380;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          11 MVSKYKYRDLTVRETVNVITLYKDLKPVLDSYVFNDGSSRELMNLTGTIPVPYRGNTYNI 70
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db           1 MVSKYKYRDLTVRETVNVITLYKDLKPVLDSYVFNDGSSRELMNLTGTIPVPYRGNTYNI 60

Qy          71 PICLWLLDTYPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHPQSDLLGLIQV 130
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          61 PICLWLLDTYPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHPQSDLLGLIQV 120

Qy         131 MIVVFGDEPPVFSRPISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPPNPSGYPGCPY 190
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         121 MIVVFGDEPPVFSRPISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPPNPSGYPGCPY 180

Qy         191 PPGGPYPATTSSQYPSQPPVTTVGPSRDGTISEDTIRASLISAVSDKLRWRMKEEMDRAQ 250
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         181 PPGGPYPATTSSQYPSQPPVTTVGPSRDGTISEDTIRASLISAVSDKLRWRMKEEMDRAQ 240

Qy         251 AELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSSALEKMENQSE 310
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         241 AELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSSALEKMENQSE 300

Qy         311 NNDIDEVIIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFLKHVRLLSRKQ 370
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         301 NNDIDEVIIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFLKHVRLLSRKQ 360

Qy         371 FQLRALMQKARKTAGLSDLY 390
               ||||||||||||||||||||
Db         361 FQLRALMQKARKTAGLSDLY 380
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Claims 1, 4-6 and 43 **remain** rejected and **new** claims 46-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Brie et al. (US 5,892,016, 1999).

Brie *et al.* teach a purified protein having an amino acid sequence having 100% identity to the amino acid sequence set forth in SEQ ID NO: 1 (Figures 1A-1B, *see* below). The patent further teaches antibodies including, but not limited to, polyclonal, monoclonal and chimeric which bind specifically to the polypeptide (column 17, line 15 to column 18, line 16). Furthermore, Brie et al. disclose that the antibodies can be used as a pharmaceutical agent for the prevention and or treatment of disease associated with expression of the polypeptide (column 16, lines 56-60). Although the reference does not specifically teach that the antibody binds to a polypeptide comprising a ubiquitination-regulating domain, the claims are drawn to the product *per se* and inherently, such an antibody would bind to a polypeptide comprising a ubiquitination-regulating domain. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

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OS   Homo sapiens.
PN   US5892016-A.
PD   06-APR-1999.
PF   23-JAN-1997;   97US-00786999.
PR   23-JAN-1997;   97US-00786999.
PA   (INCY-) INCYTE PHARM.
PI   Brie SL,  Goli SK;
SQ   Sequence 390 AA;

  Query Match             100.0%;  Score 2047;  DB 2;  Length 390;
  Best Local Similarity   100.0%;  Pred. No. 6.7e-149;
  Matches  390;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          1 MAVSESQLKKMVSKYKYRDLTVRETVNVITLYKDLKPVLDSYVFNDGSSRELMNLTGTIP 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MAVSESQLKKMVSKYKYRDLTVRETVNVITLYKDLKPVLDSYVFNDGSSRELMNLTGTIP 60

Qy         61 VPYRGNTYNIPICLWLLDTYPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHP 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 VPYRGNTYNIPICLWLLDTYPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHP 120.

Qy        121 QSDLLGLIQVMIVVFGDEPPVFSRPISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPP 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 QSDLLGLIQVMIVVFGDEPPVFSRPISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPP 180
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Qy        181 NPSGYPGCPYPPGGPYPATTSSQYPSQPPVTTVGPSRDGTISEDTIRASLISAVSDKLRW 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 NPSGYPGCPYPPGGPYPATTSSQYPSQPPVTTVGPSRDGTISEDTIRASLISAVSDKLRW 240

Qy        241 RMKEEMDRAQAELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSS 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 RMKEEMDRAQAELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSS 300

Qy        301 ALEKMENQSENNDIDEVIIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFL 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 ALEKMENQSENNDIDEVIIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFL 360

Qy        361 KHVRLLSRKQFQLRALMQKARKTAGLSDLY 390
              ||||||||||||||||||||||||||||||
Db        361 KHVRLLSRKQFQLRALMQKARKTAGLSDLY 390
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In reference to claims 1, 4, 6 and 43 being rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (IDS, US 5,891,668, 1999) and claims 1, 4-6 and 43 being rejected under 35 U.S.C. 102(b) as being anticipated by Brie et al. (US 5,892,016, 1999), Applicants assert (9/28/2006, Remarks Page 11) that the office has not met the burden of showing that the allegedly inherent characteristics (in this case, the ability of an antibody to bind to a ubiquitination regulating domain, or functional fragment thereof, within SEQ ID NO: 1) necessarily flows from the teachings of the art. Moreover, Applicants submit that one of sill in the art, reading the disclosures of either Li et al. or Brie et al., would not have recognized or appreciated whether the antibodies disclosed therein would bind to a ubiquitination-regulating domain, or functional fragment there, within SEQ ID NO: 1 because neither Li or Brie, recognized or appreciated that the full length protein had a ubiquitination regulating domain. Therefore, Applicants assert that neither of the Li or Brie documents "inherently anticipates" because the technological fact of a "ubiquitination-regulating domain" present in the full-length protein was not disclosed or recognized by either Li or Brie, both of whom clearly qualify as "technologist in the field." Further, Applicants assert that the fact that not just one, but two "technologist" failed to recognize or appreciate the presence of a "ubiquitination-regulating domain" in the full length protein is additional evidence supporting the novelty of the invention as claimed. In addition, Applicants contend that whether an antibody that falls within the scope of the claimed antibody was "accidentally" produced by either Li et al. or Brie et al. is irrelevant, as one or skill in the art would not have recognized from the disclosures whether

such an antibody was produced or not-such a recognition is required to establish "inherent anticipation." As such, Applicants submit that following the Supreme Court's long held precedent in Tilgham v. Proctor, it would be "absurd" to hold that the claimed invention to be anticipated by either of these references. Lastly, Applicants assert that contrary to the opinion of the office, similarity of amino acid sequence does not provide one of skill with the recognition required to establish "inherent anticipation" and request the office to provide citation to the Li and Brie documents showing where each of Li and Brie recognized or appreciated the presence of the "ubiquitination-regulating domain" in the full length polypeptide.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants assertions that the office has not met the burden of showing the allegedly inherent characteristic, e.g., the ability of an antibody to bind to a ubiquitination regulating domain, or functional fragment thereof, within SEQ ID NO: 1, as noted in the prior office action the Examiner concedes that neither Li or Brie et al. specifically teach that the antibodies bind specifically to the ubiquitination-regulating domain or functional fragment thereof. However, Applicants have not provided a patentable difference between the antibody presently claimed and the ones disclosed in the prior art. In the instant case, the claims 1, 4-6 and 43 are drawn to an isolated antibody that binds to a polypeptide comprising (emphasis added) an ubiquitination-regulating domain, or a functional fragment thereof, of a human TSG101 protein comprising (emphasis added) the amino acid sequence recited in SEQ ID NO: 1, wherein said antibody binds specifically to said ubiquitination regulating domain or functional fragment thereof comprising amino acid residues 50-140 of SEQ ID NO: 1, 1-140 of SEQ ID NO: 1 or 140-250 of SEQ ID NO: 1. As noted in the prior office action, the transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). In the instant case, it is

clear that the instant ubiquitination regulating domain comprises amino acid residues 50-140 of SEQ ID NO: 1, 1-140 of SEQ ID NO: 1, or 140-250 of SEQ ID NO: 1. However, there does not appear to be a patentable difference between antibodies which bind to a polypeptide fragment (100% identical from amino acids 11 to 390 of SEQ ID NO: 1) of the amino acid sequence recited in SEQ ID NO: 1 (Li, US 5,891,668, see sequence comparison) or antibodies which bind to a polypeptide that is 100% identical (see sequence comparison) to a polypeptide comprising the amino acid sequence recited in SEQ ID NO: 1, wherein the ubiquitination-regulating domain may comprise amino acid residues 50-140, 1-140 or 140-250 of SEQ ID NO: 1 because the claims do not appear to limit and/or specifically define what the ubiquitination-regulating domain consists of. As such, contrary to Applicants request that the Office provide citation to the Li and Brie documents showing where each of Li and Brie recognized or appreciated the presence of the "ubiquitination-regulating domain" in the full the length protein, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. (emphasis added) See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). Therefore, amended claims 1, 4 and 6 remain rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (IDS, US 5,891,668, 1999) and claims 1, 4-6 and 43 remain rejected under 35 U.S.C. 102(b) as being anticipated by Brie et al. (US 5,892,016, 1999). New claims 46-50 have been rejected under rejected under 35 U.S.C. 102(b) as being anticipated by Brie et al. (US 5,892,016, 1999) for the reasons set for the above.

New Rejections Necessitated by Amendment:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New claims 46-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

New claims 46 and 50 are specifically drawn to an isolated antibody that binds to a ubiquitination-regulating domain or a functional fragment thereof, wherein said domain consists of amino acids 1-250 and a pharmaceutical composition comprising said antibody of claim 46. New claims 47-49 depend from claim 46 and further limit said ubiquitination regulating domain to consist of amino acid residues 50-140, 1-140 or 140-250 of SEQ ID NO: 1. However, the specification and claims, as originally filed, do not appear to lend support for the limitation that the ubiquitination-regulating domain consists of amino acid residues 1-250, 50-140, 1-140 or 140-250. For example, Applicants submitted that support for new claims 46-50 can be found on page 2, line 20 to page 3, line 9 of the specification as filed and in original claims 1, 4-6 and 43. However, the specification on page 2, line 20 to page 3, line 9 and original claims 1, 4-6 and 43 only appear to lend support to a ubiquitination-regulating domain comprising amino acid residues 1-250, 50-140, 1-140 and 140-250 of SEQ ID NO: 1 which is different from a ubiquitination-regulating domain consisting of amino acid residues 1-250, 50-140, 1-140 and 140-250 of SEQ ID NO: 1 (*see* MPEP, 2111.03). Applicant is invited to point to clear support or specific examples of the claimed limitation in the specification as-filed or remove such amendatory language in response to this office action.

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Conclusion

Therefore, NO claim is allowed

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the

THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

BF

SHANON A. FOLEY
SUPERVISORY PATENT EXAMINER